**I No wall (Mollicutes):** smallest microbe, passes through 0.45 micron filters, 1/5 genome of *E.Coli.* Triple cell membrane with sterols (*Mycoplasma (3), Ureaplasma)*

1. *Mycoplasma Pneumoniae* [1-3 weeks]: **SX**1⁰ atypical pneumonia (5-20yr olds), tracheobronchitis (under age of 5) caused by the spread of respiratory droplets. 20% asymptomatic, IgM develops 7-10days post infection. Epidemics every 4-8 years and peak seasons are summer and fall even though not seasonally based. Aerobic, fastidious, special media to grow “fried egg” looking colonies(still 2-6wks), degenerative genome possibly from g(+). P1 adhesin moderates the binding of the bacterium to the TLR-2 at the base respiratory epithelial cell cilia. P1 shows antigenic variation as a result of homologous recombination between the 7-25 various P1 repetitive elements. After attachment, mycoplasma release H2O2 and O2- to impair cilia causing desquamation. Additionally, the entire bacteria acts like an antigen and causing a vigorous host immune response from lymphocytes, antibodies, cytokines… **Diagnosis/TX: Chest xray, ELISA for antibodies, culture to confirm (no good for diagnosis do to long culture time), possibly a cold agglutination test or sputum test (agglutination is not very specific or sensitive and the patients have little sputum for a sputum test). Macrolide/Tetracyclines/Quinolones are all treatment options (currently no resistance and no vax available)**
2. Extrapulmonary *Mycoplasma Pneumoniae*: autoimmune response generated against the cholesterol on host cell surface
   1. 25% Rash: erythema multiforme (mild cases) or Stevens-Johnson syndrome (severe cases). Damage to the microvasculature and dermal layers
   2. 14% Nonspecific myalgia/arthralgia: persist even weeks post disease
   3. 6-7% CNS: encephalitis, cerebellar syndrome, meningitis, confusion, CNpalsies (all have antibodies to myelin)
   4. Reynaud’s phenomenon: vasospasm when digits exposed to the cold
   5. 1-8% Cardiac problems: pericarditis, myocarditis, conduction, heart failure
   6. Associates: Guilliane barre (5-15%) Asthma (56% cultured vs 9% controls) COPD (6-14%)

NOTE: Patients with hemoglobinopathies have more severe complications like digital necrosis

1. *Mycoplasma hominis/genitalium*: T-strain, in 15% of sexually active people. See details below… does cause 10% of PID and abortion/postpartum fever without sepsis for 24 hrs. **Diagnosis/TX: clinical presentation is enough to diagnosis and prescribe clindamycin; resistant to erythromycin and tetra**
2. *Ureaplasma*: T-strain, 45-75% of sexually active people. **SX:** Its unique urease allows it to hydrolyze urea to reduce its toxic effects on the microbe allowing the microbe to colonize the urethra and cause urethritis (20% of cases), cervicitis, endometritis, PID, pyelonephritis and abortion/postpartum fever. Both M.hominis/genitalium and Ureaplasma can be transmitted vertically (colonization decreases beyond 2yrs and increases again at puberty). Affects the respiratory tract in neonates (usualy cleared by maternal antibodies) **Diagnosis/TX: clinical presentation and possibly a urine culture. Treat with erythromycin; resistant to tetras**

**II Spirochetes:** nontoxic, highly invasive, damage is mediated by the immune response. Super long and super thin… thus they will need dark field microscopy to be seen. These are unique because they have endoflagella that are inadequate for locomotion in aqueous solution but fantastic for dense tissue. They could be considered a derivative of a g(-) because they have two membranes and a cell wall. However, they do not have LPS or lipotechoic acid and have few outer membrane proteins (only a few porins and lipoproteins). (*Borrelia (4 kinds) Leptospirosis(200 serotypes), Treponema)*

1. *Borrelia burgdorferi* (days to weeks):
   1. Ticks serve as both a natural reservoir and vector. The bacteria cannot be transferred transovarially so the tick larva need to have a maintanence pool in the wild (mice and humans). The larva feeds on an infected mouse and then becomes infected itself. The larva molts to a nymph and still the bacteria persists. The nymph feeds on mice and humans and transfers the bacteria and allows maintanence of the natural pool. The nymph molts to an adult which no longer possesses an active bacteria but still need to survive to reproducing state where more larva can be generated. Deer provide the necessary food supply to survive to the reproductive stage. Bacteial infection occurs in youths and middle aged adults during the active tick season. *Ixodes scapularis* and *Ixodes pacificus* are natural hosts of the bacteria but the *scapularis* are the primary vectors to humans since *pacificus* do not seem to feed on humans as much. Additionally, the *pacificus* feed on lizards which have yet to become capable of carrying the bacteria and their immune systems kill it immediately.

**SX** include bulls-eye rash (erythema migrans 60-80% of cases), flu like symptoms occurring days to weesk post infection. 99% are cured if treated appropriately. HAS MANY LIPOPROTEINS used for different host environments. 21 genomic plasmids (9 circular 12 linear with 90% of the genes being unique to this bacteria). Virulence is attributed to: huge variation in surface proteins which can be limited to the internal membrane, endoflagella, adhesions, complement inhibition by Erp, hiding behind the proteins in tick saliva, plasminogen binding (prevents clotting), and using magnesium instead of iron. **Diagnosis/TX: erythema migrans with known exposure is an automatic… if not must have one of the subsequent manifestations and lab evidence by isolation of the bug, Elisa/western or IgG titer. Confirmed disease, probable disease (labs but no clinical evidence), suspected (EM but no evidence or lab tests without any clinical data). Give oral amoxicillin, cefuroxime or amoxicillin for a few weeks. IV ceftriaxone or IV penicillin given in CNS and cardiac cases. No vax**

1. *Secondary Borrelia burgdorferi*/Subacute Lyme Disease(weeks to years post 1⁰ infection): transient sequela occur after the microbe disseminates to various tissues. The symptoms respond to antibiotic treatment, spirochetes can be detected in the tissues, not MHC associated, inflammation driven by intrinsic response to lipoprotein. These are:
   1. arthritis (60% SX ↑synovial tissue, macro/neutro invasion… but no B/Tcells)
   2. neuro (20% SX show bell’s palsy, lymphocytic meningitis, radiculoneuritis)
   3. cardiac (8% SX with AV block, myocarditis, palpitations)

NOTE: chronic Lyme disease is different than a Subacute. Chronic is mediated by an autoimmune response. The symptoms resist treatment, there are no spirochetes still detectable, specific HLA involved and Tcell involvement

1. *Borrelia hermsii/duttoni:* the arthropod vector, *ornithodoro*s (Soft ticks in the western US), **SX** cause endemic relapsing fever that has a low fatality. Bug replicates in the blood and neural tissues and can cause Jarish-Herxheimer rx due to release of lipoproteins. **TX: tetracyclines**
2. *Borrelia recurrentis:* the human body louse (endemic to Africa and S. America) causing **SX** epidemic relapsing fever, has a higher fatality rate and also replicates in the blood. **TX: tetracyclines**

NOTE: both have reoccurring fever spikes. The bacteria has a variable membrane protein VMP that can be shuffled causing constant evasion of the host immune system. **Diagnosis: peripheral blood smear, bone marrow, CSF in darkfield microscopy (best if samples from a febrile individual). Normal WBC but a left shift, mild rise in bilirubin, mild to moderate thrombocytopenia. Erythromycin, tetra, chloramphenicols and penicillins have all been found effective TX.**

1. *Leptospirosis:* **SX** initial phase of flu-like symptoms that are transient. Secondary disease includes: aseptic meningitis, fatigue, liver damage (jaundice), red eyes, hearing loss, resp/cardio. There are over 200 sero types correlated to specific LPS structures. Bug is shed in the urine of the infected host (rodent, raccoon, dogs, cattle…). Contracted by contact with contaminated water or soil… also by direct contact with the urine or body fluids of an infected animal. The bacteria penetrate the hosts defenses by drilling through the skin or mucous membranes (eyes, kidneys, liver). Some develop sever renal/liver dysfunction with a high mortality rate (Weil’s Disease) or Severe Pulmonary Hemorrhagic Syndrome (SPHS). **Diagnosis/TX: agglutination, cultured in highly enriched liquid or agar to produce slow growing colonies. Administer Doxycycline or B-lactams. (A lot of the cases come from Hawaii or Brazil) MOST WIDESPREAD ZOOTONIC DISEASE IN THE WORLD.**
2. *Treponema (10-90 days):* NO ENDOTOXIN… most lipoproteins are on the inner membrane. Sexually spread and no known animal reservoir. Cannot be grown on any lab medium but can be injected and grown in rabbit testicles. Mostly from men having sex with men (60%). May have originated from the condition called Yaws in Africa. That disease is spread by skin/skin contact and rarely causes visceral or nervous system infection. **SX** Syphilis is far more invasive and is carachterised by a chancre (“Kanker”). 1⁰ vaginal chancre that is plainless and heaped at the edges, lasts a few weeks and neutrophils are present (later replaced by macro/lymphocytes). 2⁰ dissemination through the blood causing fever, malaise, arthralgia new cutatneous lesions (great pox) on the palms, hands, soles and hepatosplenomegaly. 3⁰ 30% of patients with granulomatous lesions called gummas which occur in the skin, bone and liver. Can cause general paresis with dementia and paralysis, cadio syphilis with aortic aneurysms or tabes dorsalis if posterior column of spinal cord is lost, resulting in a lack of coordination, sensation, nutrition…. **Diagnosis/TX: cannt be grown in artificial medium so use serologic methods or PCR. Also can monitor cardiolipin (other diseases will have a positive CL test like malaria, leprosy, measles, lupus… and still false negatives if the bacteria is latent or in 3⁰). Use immunochromatography. CONFIRTMATION: FTA (fluorescence), TPHA, TPPA (agglutinations). Treat with a 1x shot of PenG. NO resistance but no vax.**
3. *Congenital Treponema:* mother is the reservoir with transplacental infection. No infection during the first 10 weeks of pregnancy (provides a treatment window); early pregnancy infection results in miscarriage; late pregnancy infection causes moon’s molars, congenital defects, skin lesions, bone deformation…

NOTE: Treponema evades the immune response by coating themselves with: albumin, transferrin, IgG heavy chain, MHC I. Only real proteins they display on their outer membrane are TROMPS. It also has 22 different lipo proteins (characteristic of sphirochetes to have large numbers of lipoproteins. Realize the correlation between the stages of treponema pallidum and borellia burgdorferi

**III Gram Positive: Rod (sporulating/non), Coccus, Pleomorphic, Actinomycete**

**🚑 Rods:**

1. *Mycobacteria*: Non sporulating hydrophobic barrier made of mycolic acids (acid fast stain), cause tubercles in the lung, non-motile, obligate aerobes. Slow growth, L-J media or Middlebrook’s media (Note that leprae cannt be cultured). Can survive weeks/months on inanimate objects. Resist freezing or drying but not UV or heating
   1. *M.leprae(20yr latency):* Leprosy/Hansen’s disease mostly in Angola, Brazil, DR, Congo, India, Madagascar, Tanzania, Nepal. Transmitted by droplets to the nose/mouth. No natural reservoir but some armidilos seem to carry the bacteria. **SX** hypopigmented tissue that becomes flat macules -> large papules -> nodules. **Diagnosis/TX: acid fast skin biopsy and symptoms. Treat with rifampicin and dapsone (pteridine synthesis inhibitor) for 6 months and clofazimine for severe cases (12 months)**
   2. *M.avium and M.intracellulare:* normally in soil, water, plants, animals… Very common for HIV patients to develop MAC in the lungs but can also develop in the GI and lymphnodes. **SX** TB like nodules in the lungs, cough, fatigue, weight loss. 45-60 yr old men or Lady Widermere syndrome in old ladies who wouldn’t cough. **Diagnosis/TX: PCR of lavage (positive result does not mean disease unless the clinical symptoms are present and xrays indicate nodules). Treat with ethambutol, rifampicin and clarithromycin/azithromycin.**
   3. *M.marinum/M.ulcerans:* trauma followed by exposure to dirty water (SE Costal US and Africa/Australia wetlands). **SX** painless lumps develop into full limb deformities. **TX: Rifampin and ethambutol**
   4. *M.tuberculosis*: *(complexes include M.bovis/africanum/caprae/microti)* traditionally called consumption. Currently 30% of the world populous is infected. 5-15% develop active disease. Need prolonged contact to contract the bug from respiratory droplets. **SX:** Cough with mucus/blood, chest pain, night sweats, weight loss, fatigue, low fever. Early stage: translocation through lung epithelium to alveolar dendritic cells/macrophages to bind to Fc, CR, Mannose receptor, LDL scavengers and enter. Tcells secrete IFN gamma. Macrophages and B/T cells encapsulate and the bacteria goes latent (non-replicative/low metabolism inside the caseum core of the granuloma). Late stage: the granuloma breaks open and the contents spread. **Diagnosis/TX: sputum stain in the early morning, skin test by PPD, culture in MGIT, QuantiFERON uses blood and will show positive results if the sample has tcells releasing IFN-y in response to the secreted antigens not present in vax. Treat with 6-9 months of Isoniazid+Rifampin+Pyrazinamide+ethambutol (first 2months go hard and then phase out the last two drugs). If extensively resistant, treat with fluoroquinolones and second line oral drugs like kanamycin, amikacin and capreomycin. There is a vax derived from the *M.bovis* strain. This is not used in the US since it has side effects, incomplete protection, only prevents childhood disease and interferes with skin testing.**

NOTE: Virulence factors for TB include LAM (mannose core, arabinose side chains and mannose cap to bind to the macrophage and inhibit activation by preventing phagosome fusion with lysosomes). Transferrin is recycled and LAM binds to other neighboring macrophages to inactivate them as well. Mycolic acids form thick barrier to protect from UV, dessication and compliment/neutralizing antibodies. TDM cord factor is a glycolipid that attatches to the mycolic acids to interfere with phagosome maturation and damages mitochondria and neutrophils. 19 lipoprotein suppresses TNF-a, IL12, MHCII and induces apopltosis in late stage of infection. PDIM peripheral lipid that is shed (like LAM) to interfere with MHCII loading.

1. *Listeria monocytogenes:* usually acquired in food and elderly or immunesuppressed are at risk**SX** 7-10 day fever, invasion of intestinal epithelium, growth within macrophages, septicemia, meningitis/encephalitis, corneal ulcers and pnuemoia. Can cause intrauterine infection resulting in granulomatosis infantiseptica (pyogenic granulomas). High mortality rates. Convergent evolution with *Shigella.*  Invasion, hemolysin, growth, actin based motility (ABM), release with adhesion attachment. **Virulence** this bug has N-deacetylation of the side chains of PG to prevent degradation by antibiotics and host defenses. Also can grow at a wide range of temps, acids, salts. Motile at room temp and weakly hemolytic. **Diagnosis/TX B-lactams with aminoglycosides as well as avoiding foods that have high rates of contamination (cheese, raw veggies, processed meat).**
2. *Bacillus antracis:* Sporulating1877 discovered to cause disease, vax for animals in 1881. Facultative anaerobe (other Bacilli can be strict anaerobes). Has a toxin with 3 components. Protective antigen (PA) binds to a cellular receptor where it is cleaved by a protease. The cleaved product self associates with other PA molecules to eventually form a heptameric prepore with up to three molecules of Edema factor (EF) and/or Lethal factor (LF). The complex will be endocytosed, exposed to H+ which causes the prepore to activate and translocate EF and LF to cause edema and cell death. The endospores are long ellipsoids in the center of the bacteria (which aggregate as chains or sit individually). The bacteria have a prominent protein capsule of poly-D glutamic acid. **SX** INOCULATION: Spores are introduced through exposed skin creating a painless papule -> ulcer -> necrotic eschar (mortality is 20% in untreated cases). INJESTION: upper GI ulcers, swollen lymph nodes and sepsis; lower GI, nausea, malaise, systemic disease. INHILATION: infected alveolar macrophages then enter circulation. Mediastinal lymph node enlargement, widening of the aortic arch and 50% with meningeal involvement/shock. High mortality even in the treated patients. Death in 1.5-3 days. **Diagnosis/TX Microscopic examination reveals bacterium. Culture shows the endospores and a confirmation stain to see if the bacteria possesses the appropriate poplypeptide capsule. Need Biochem assays and serology tests for reporting puposes. Treat with several different antibiotics immediately (cipro, doxy, amoxi). Some vax available but not necessarily effective against inhaled bacterial spores and needs boosting**

NOTE: Capsule pXO2 is non-toxic but protects the bacteria from phagocytosis. Anthrax toxins pXO1 (PA, EF, LF)

1. *Bacillus cereus:* aerobic or anaerobic with spores found everywhere. Common cause of food-borne intoxication with transient, self-limiting illness of 24hrs. **SX** Short incubation is 1-6 hours with nausea, vomiting, cramps and due to the toxin… not the bug (Looks like *Staph. Aureus*). Associated with milk, rice, pasta. Long incubation caused by consumption of spores followed by heat-labile enterotoxin production in the small intestine. These include camps and diarrhea within 8-16 hours due to increased cyclic AMP. Occular infection following trauma of the eye and blindness in 48 hours (*B.thuringiensis* can also cause this). **Diagnosis/TX Do not require thiamin, cause hemolysis, no “string of pearls”, motile, grown on chloralhydrate agar. NO TREATMENT NEEDED unless its supportive treatment in very rare cases.**
2. *Clostridium botulinum*: Strict anaerobe, common in animal GI tract. 7 toxogenic types of which A is the most common in the US. The binary toxin is a single chain that is cleaved to the dichain molecule connected by disulfide bridge with A being a zinc eendopeptidase. B provides cholinergic specificicy. The toxin will bind the presynaptic terminal where it is quickly taken in. A will cleave the peptides needed for Ach release resulting in flaccid paralysis. **SX** Infant botulism (1-2month old): spores germinate quickly in the baby’s naïve intestine. Symptoms start with the waiste and work their way up. First sign is constipation and antibiotics are not recommended though an antitoxin can be administered. Wound botulism: bacteria in the infected wound produce the toxin (mostly drug users). Food borne (symptoms at 6h-2wks): injested toxin from improper canning. Symptoms start with the neck and work their way down. Dry mouth, slurred speech, muscle weakness… DON’T EAT BEACHED MARINE MAMMALS Terrorism: aerosolized toxin is a possible threat. Iatrogenic botulism: the result of overdosing at botox parties. **Diagnosis/TX typical diagnosis by clinical evaluation. Can be confirmed by stool tests but this takes days and not very effective. Treat with antibiotics if wound botulism. Recovery depends on the regeneration of new nerve endings and patients require supportive therapy in the meantime. Equine based antitoxin for food borne or human recombinant antitoxin for babies. Vax not recommended. Proper food preparation is advised with using vinegar/acids to cook with and heating your food 80C for 20min to kill endospores or 10 min heating to kill the toxin.**
3. *Clostridium tetani (3-21 day incubation):* round terminal endospores (as opposed to centrally located spores in anthrax). Very sensitive to oxygen as it quickly triggers sporulation. Ubiquitous in soil, animal gut… Two toxins are Tetanolysin (oxygen labile) and Tetanopasmin (heat labile) of which the second is the AB toxin and plasmid encoded. Spores enter by a wound where they grow in anaerobic conditions. Toxin is produced in the stationary phase and released when the cell lyses. The toxin is cleaved to 2 chains and B binds to neuronal membranes while A is internalized into the axon and travels to the CNS by retrograde transport. Fixes itself to gangliosides and cleaves synatptobrevin II to inhibit GABA and glycine release. **SX** muscular spasms, better outcome the further the injury is from the CNS. Localized tetanus has persistent muscle contraction at the site of injury. Cephalic tetanus: cranial nerves, otitis media, uncommon but usually poor outcomes. Generalized tetanus: (80%) present with trismus (lock jaw) followed by stiff neck, trouble swallowing, fever, spasms for 3-4 weeks. Neonatal form is seen in infants born to nonimmunized mothers. **Diagnosis/TX entirely clinically based. Need to debride the wound and issue metronidazole. Antitoxin can be given early in the disease course. Prophylactic immunization by tetanus toxoid (DTaP is dipteheria, tetanus and pertussis). 4 doses then a 5th at 4-6, a booster at 10 then every 10 years.**
4. *Clostridium perfringens:* used to be the most common but now being out paced by difficile. Anaerobic, non-motile, highly metabolically active, easy to identigy in lab and 5 strains based on the toxins. Widely distributed in the intestinal tract and fecal contaminated water. Alpha toxin is the most important as it causes cell lysis and vascular permeability. Beta toxin causes necrotic enteritis. Epsilon toxin is cleaved to increase vascular permeability. **SX** food poisoning with symptoms being shown at 8-24 hours. Consumption of infected food with type A vegetative cells causes the production of enterotoxin (Alpha toxin) leading to cramps and diarrhea. Necrotic enterotoxin (Beta toxin) is released by type C. The bowels die and bacteremia ensues. Mostly in New Guinea where the combination of uncooked pork with sweat potatoes exacerbates the situation. Cellulitis is an infection of skin/connective tissue that is already dead. Little pain but forms crepitance (gas pockets). Has a good prognosis. Gas Gangrene (myonecrosis) is an initial trauma that impairs blood supply creating optimal anaerobic conditions. Fever, intense pain in the infected tissue purple mottling, edema, foul smell (N2 from fermenting bacteria). Causes shock and renal failure leading to death in 48hrs. **Diagnosis/TX lab confirmation post treatment includes a tissue culture. Needs surgical debridement and high doses of penicillin. Only the food poisoning has a limited impact.**
5. *Clostridium Difficile:* common nosocomial infection with individuals who have been on extensive antibiotic treatment resulting in the removal of the natural flora populating the colon. The bacteria are opportunistic. Toxin A (enterotoxin) is chemotactic for neutrophils causing inflammation and some cytotoxicity. Toxin B (cytotoxin) causes actin depolymerization and cytoskeletal destruction. The A targets the apical membrane and breaks the tight junctions while the B (more destructive) targets the basolateral membrane. **SX** pseudomembranous colitis results from uncontrolled bacterial growth resulting in leukocyte infiltration into the lamina propria, elaboration of fribrin, mucus and leukocytes all while creating a thin membrane throughout the mucosa. **Diagnosis/TX clinically significant diarrhea for 1-2 days AND be an at risk patient, positive lab test (culture but it takes time, PCR but its expensive and doesn’t rule out the natural flora, ELISA is really the best even though its not that sensitive or specific, colonoscopy is to invasive especially if the patient has tin colon wall). Treat by stoping offending antibiotic, supportive therapy, metronidazole 1st then vancomycin 2nd (maybe a new drug coming). Realize that relapses can occur (10-50%) and monoclonal antibodies are being tested for toxin A and B. NOTE some studies suggest decreases in acid production can cause spores to germinate.**

**🚑** **Coccus**

1. *Streptococcus :* some secrete toxins others are non-toxin producing. Classified based on hemolysis (alpha beta gamma), group specific carbs (lancefield groups), biochemical characteristics (catalases…). Alpha create green colonies since they can lyse the cells but cannt take up the iron. Beta induce complete hemolysis. Gamma have not observable hemolysis.
   1. Group A Beta Hemolytic Strep GABHS: *S. pyogenes-* Groups A and C based on their specific carbohydrate capsules. Spread by contact with carrier (20% of school age carry) or aerosol. Group A and is subject to the agglutination rapid strep test and also bacitracin sensitive. Have M prtein with a hypervariable region allowing the bug to display 130 different serotypes. The antibodies bind to the amino-terminus, the distal portion of the M binds fibrinogen to block the complement path, proximal portion binds factor H blocking the alternative path. Host defense is opsonization with phagocytosis by neutrophils and cleared by complement. **Virulence:** Adherence of keratinocytes and binding fibronectin; Evading immunity by hyaluronic acid capusule and binding Ig; Invading the tissues with hyaluronidase, DNase, Streptolysins/kinases; Strep toxic shock by pyrogenic exotoxins and super antigens to stimulate t cells. **SX** fever, no cough, swollen lymph nodes, tonsilar swelling/exudate and young. Can also have headache, nausea, vomiting, raspberry/strawberry tongue with soft palate petechiae. **Diagnosis/TX culture from tonsils on blood agar (1-2 days), g(+) chains, Beta hemolytic and bacitracin sensitive; Rapid Antigen Detection Test (RADT) by agglutination (group carb) or optical immunoassay; DNA PCR for M protein. Administer PenV oral for 10 days (MUST COMPLETE DOSE), Benzathine penicillin G IM, Cepha or macrolides if penicillin allergies. Also recommended to give Ibuprofen or acetaminophen. DO NOT ALLOW KID TO RETURN TO SCHOOL FOR 24 HOURS. If no antibiotics it can persist for +6 weeks and cause:**
      1. Scarlet Fever: toxin mediated (Exotoxins Spe A,B,C) in the blood stream. A and C encoded on a prophage in the chromosome and are superantigens. B is a protease that cleaves host and bacterial proteins. Usually arises from pharyngitis but can come from the skin and is very serious. **SX** Fever 107-8C, severe headache, sandpaper rash on day 2 on the upper trunk then to the rest of the chest. Occlusion of sweat glands causes the maculopapular rash resembling sunburn (PT have circumoral pallor). Also havepastia’s lines on neck, elbow, stomach, underarm… Desquamation during second week of illness.
      2. Impetigo/Pyoderma: **SX** localized and purulent infection of the epidermis in children with poor hygiene. Mostly in summer months of a northern climate or all year in a tropical climate. Colonization of the skin (10days and asymptomatic) followed by invasion after trauma. The papules become pustule with a honey colored exudate (staph bullous impetigo has a clear crust). Usually self-limiting but can prescribe penicillin or mupirocin
      3. Erysipelas: deep infection of dermis following pharyngitis. **SX** acute inflammation with lymphatic involvement (face, trunk, extremities but the face is the least problematic). Visible, raised, advancing red margins. Can be fatal and treated with penicillin.
      4. Cellulitis: **SX** deep infection in the dermis that is acute spreading from a wound/burn/surgery. Local pain, erythema and swelling that expands to become large areas of redness (without a clear margin) as the bacteria go systemic. Use penicillin.
      5. Necrotising Fasciitis: **SX** deep infection of the dermis with extensive and rapidly spreading necrosis. Mortality can be high. Begins after an inapparent trauma, extensive spread in 24-72h. Intense pain with skin turning to very large bullae (filled with yellow fluid) and dark purple skin. Bacteremia with gangrenous sloughing skin. **Virulence: Hyaluronidase, M protein, Hemolysins O and S.** High fever, extreme prostration, rapid/bullous inflammation needing IV antibiotics and surgical debridement.
      6. Staph Toxic Shock Syndrome: **SX** Unlike Staph aureus which sends its TSST-1 toxin into the blood stream, the GABHS actually enters the blood to produce super antigens causing the fever, rash, shock, NF and 30% mortality. Can start from almost any location. A and C are though tot mediate the pathogenesis. Mostly in adults with sporadic and small outbreaks with person-person spread. **Diagnosis/TX isolate from a normally sterile site or a non-sterile site, identify hypotension with 2 additional clinical symptoms (Renal/Liver, blood coag impairment, respiratory distress, rash, soft tissue necrosis). Administer pen G and clindamycin. Clindamycin is better since it is bacteriostatic and would not cause cell lysis.**
      7. Randoms: Pneumonia, Puerpural Sepsis (invasion of the endometrium/lymphatics/blood post abortion/partem), Lymphangitis (with cellulitis or skin infection where you have linear streaks towards regional lymphnodes and chills/fever/headache.
      8. Acute Rheumatic Fever (1-4 wks): post GABHS infection, no bug present, immune mediated. Only follows pharyngitis. Repeat attacks occur when encounter a new strain of the bug. Usually age 5-15. **SX** poly arthritis (large joints), carditis, chorea, erythema marginatum, subcutaneous nodules, and MAYBE fever, arthralgia, acute phase reaction, increased sedimentation rate, CRP. Rheumocarditis will have increased heart size with pancarditis. Can have a murmur and chronic valvular heart disease. Arthritis alone is not a classic presenting feature. Chorea is the rapid involuntary and non-repetitive movements. Need to be on prophylactic pen V or pen G for 5 years or atleast till the age of 25
      9. Post strep Glomerulonephritis (1-4 wks): all ages but mostly kids where the immune complexes are not cleared by compliment system and accumulate in the glomeruli. **Diagnosis/TX Dark urine with protein, headache, back pain, edema, hypertension all presumptive diagnoisis. Biopsy and Anti-dnase test are used as definitive methods for diagnosis. Administer penG, supportive care which will ultimately most likely include dialysis.**
   2. Group B Strep (GBS): *S.agalactiae-* bacitracin resistant but beta hemolytic. Capsule polysaccharides have 9 serotypes that block phagocytosis. MAC can bind but the oligosaccharide subunits are so thick that it is ineffective. Also display sialic acid (mimicry). CytolysinE pore forming toxin causes tissue damage and bacterial spread by killing neutrophils. **Virulence:** binding, invade epithelial cells (even Brain), direct cell injury, resist phago/intracellular killing, activate inflammation, CNS neutrophil recruitment. **Scan mothers at 35-37 weeks** since 25% have the infection, 60% of the babies will then be colonized of which 1-2% have early onset disease with fulminant pneumonia, septicemia and high mortality or late onset meningitis, osteoarthritis, cateremia. Adults show skin infection (cellulitis), primary bacteremia (mortality 50%), pneumonia (opportunistic), meningitis (rare), endocarditis to the mitral valve, septic arthritis (at the knees with 10% mortality). **Diagnosis/TX with vaginal and rectal swabs to perform a camp test with S.aureus to see if the GBS enhances the hemolytic activity of S.a. Treat with Pen/Amp and often combined with aminoglycosides or cefazolin. Can also do Vanco or Clyndamycin if allergic. IV Pen G 4 hours before delivery in infected women. Erythromycin and Tetra are resistant. Vax is not currently used**
   3. *S.pneumoniae:* almost 60% of pneumonias, MOST DAMAGE IS HOST IMMUNE RESPONSE even though it does produce H2O2 and Pnuemolysin. Colony phenotypes are lancet/diploid shape on blood agar. It is alpha hemolytic (not beta) and also optochin sensitive (this makes this strep its on class since it does not fall into the lancefield groups. Colonizes the nasopharynx from contaminated respiratory droplets. Infections are mostly in kids though most people are colonized at 6months. Disease is the result of an exposure to a new serotype. The pneumonia is serious in adults. **SX** bacteria grow in the edeam in the alveolar space. It is rapid with a productive rust colored cough. Also fever, chills, chest pain and x-rays show singular, lower lobe involvement. Causes 1/3 of all meningitis. Also causes 40-50% of otitis media in kids (often predicated by a viral infection). **Virulence: Pneumolysin** is secreted and forms pores in ciliated epithelium of the lung, phagocytes and degrades hemoglobin while activating complement. Its IgA Protease cuts the Ig to release Fab fragments that opsonize the bacteria but cannot bind to the Fc receptor. Neuramidase and Hyaluronidase allow the bacteria to thicken mucus, to remove sialic acids from cell surface for adherence and to travel in the extracellular space. Capsule is antiphagocytic. Also soluble capsular fragments are released to recruit neutrophils to increase inflammation and cause an increase in the permeability of BC so the bacteria can induce bacteremia. The capsular proteins also vary depending on the stage of the infection thus allowing the cell to escape adaptive immune response. Autolysin is another enzyme that breaks down its own cell wall to cause the cell to lyse and release PG fragments to increase inflammation and also cause bacteria to become competent to take up the destroyed bacteria’s DNA. Also has choline binding proteins to sequester choline for its membrane and surface proteins to inhibit complement deposition. **Diagnosis/TX blood agar culture will show diplococcic, hemolysis alpha, optichin sensitivity, and opaque (increased capsule and surface protein needed for virulence) or clear (increased persistence, rapid autolysis) colonies. Treat with levofloxacin or vanco since very resitant. Need to just control the spread until the patient’s immune response can finish. Vancomycin resistance has not been observed. Conjugated vax show promise though need continual updating**
   4. *Enterococcus faecalis/faecium:* alpha hemolytic or non hemolytic. Commensals grow in very harsh conditions like bile salts, UT, vagina. Nosocomial with limited virulence but can be life threatening. **SX** UTI with dysuria, pyuria; Peritonitis from a wound or surgery; Endocarditis persistant, acute, or chronic. HIGH GENETIC TRANSFER and house many antibiotic resistant plasmids. **Diagnosis/TX**
2. *Staphylococci:* Micrococcae family, catalase producing, facultative anaerobes. Some produce coagulase (CPS) and some do not (CoNS). In general, CPS are beta hemolytic, CoNS are gamma hemolytic. Typically seen in clusters (tetrad) on an agar plate. They are non-motile, non-spore forming but they do make exotoxin.
   1. *Staph aureus:* major human pathogen, yellow colony appearance comes from the production of carotenoids. PG, teichoic acid, protein A are all cell wall components. The PG causes the production of IL-1, attact PMN, activate complement and antibody response. The techoic acid has two types and unknown pathogeneity. Protein A binds the Fc terminus of IgG. This bacteria conlonizes humans at birth (10% of females show vaginal collinization). **Virulence:** dictated by the agr gene. Teichoic acid helps bind to mucosal cells; fibrinogen/fibronectin/laminin/collagen all play roll in binding to traumatized skin; fibronectin and laminin allow adherence to endothelial cells. After infection, they create an abcess from the release of proteases, catalases, coagulases (2 forms: bound and free). Hemolysin, hyaluronidase, B-lactamase, exfoliates (scalled skin syndrome) cytotoxins are some key enzymes. SUPER ANTIGETNS: TSST1 and enterotoxins A-E bind and activate the Tcells for poly clonal activation/amplification. **Diagnosis/TX: coagulation tests in rabbit plasma or staphaurex test with rabbit IgG and latex beads. Job’s/Chediak-Higashi/Wiskott-Aldrich syndromes predispose to contracting a staph infection as well as Chronic granulomatous disease. Infection induced disease can be Toxin determined, Localized, or Systemic. Examples include**
      1. *Food poisoning:* [2-6 hrs] with enterotoxin A or B in foods left at room temp. Abrupt salivation, N/V/D, community out break and self-limiting.
      2. *Toxic Shock Syndrome:* colonization leads to toxin production when the bacteria encounter an environmental stress. Seen post-surgical procedures and women using tampons. Desquamation on the feet and hands is symptom.
      3. *Folliculitis:* inflammation leads to furuncles then carbuncles then hiradenitis
      4. *Impetigo:* see previous descriptions except crust is clear
      5. *Cellulitis:* see previous descriptions
      6. *Lymphagitis:* see previous descriptions
      7. *Scalled Skin Syndrome:* Ritter von Ritterschein causing generalized skin sloughing or localized blistering. **\*\*\* Needs to be differentiated from TEN which has the same symptoms but is autoimmune related and needs diff treatment.\*\*\***

**Treatment needs to be accurate. Drain pus if possible, remove forein bodies, administer antitoxin, treat with antibiotics for +4 weeks**

* 1. *MRSA:* Community acquired mrsa is a strain that carries PVL toxin on a mobile phae and is associated with skin, soft tissue infection and severe necrotizing pneumonia with sepsis. Hospital acquired mrsa has a larger cassett and more antibiotic resistance Use pulsed field gel electrophorese PFGE with rare cutting restriction enzymes to find the epidemiology of the strain. **Diagnosis/TX: need to run PFGE to find the strain and then administer doxy, linezolid, vancomycin if community acquired (can add rifampin too but resistance develops quickly). IF hostiptal acquired, vancomycin unless it is resistant and then you will need to administer linezolid or daptomycin. Run a susceptibility test to know which drug.**
  2. *Staph epidermis:* normally in 65-90% of people. VERY antibiotic resistant and represents nearly all of the nosocomial infections. It is coagulase negative and gamma hemolytic. Biofilms (exopolysaccharides) allow this bacteria to contaminate “hardware”. This is the agent responsible for prosthetic joint infection and sternal osteomyelitis postsurgery. It rarely infects native valves but causes 40% of prostethic valve endocarditis. **Virulence:** the biofilm protects from opsonization, antibiotic penetration and some of the surface antigens will prote its adherence. **Diagnosis/TX: line sepsis requires vancomycin. Infectious endocarditis needs multiple sets of positive blood culture, clinical suspicion, and echo. Endopthalmitis can also be seen and needs IV vanco and itravitreal antibiotics. UTI in elderly hospitalized with catheters.**
  3. *Staph hemolyticus:* resident in the skin and mucosal membranes. Everything similar to epidermis
  4. *Staph saprophyticus:* truly a urinary tract pathogen and similar UTI presentation as GNRs like E.coli. Often in women not long after sex. **Diagnosis/TX: Bactrim and quinolones.**
  5. *Staph lugdunensis:* this is a particularly aggressive CoNS (is actually beta hemolytic though) that is infrequent but causes aggressive endocarditis, CHF, and high mortality. **Virulence:** has PYR which is some crazy enzyme useful to diagnose… also rapid ornithine decarbxlase.

1. *Peptostreptococcus:* normal part of skin, oral, URT, GI, female genital tract. Opportunistic anaerobic bacteria that causes abscesses, NF, plueropulmonary infections

**🚑** **Pleomorphic: Coryneform bacteria (corynebacterium (6types), arcanobacterium, brevibacterium, rothia, tropheryma) and Propionibacteria**

1. *Corynebacterium diptherieae (2-5 days):* club shaped, high G-C content, non-sporulating, facultative anaerobe, non-motile and cell wall has short chain mycolic acids (like mycobacteria). Grow in clumps that look like “Chinese letters”. Metachromic granules that contain inorganic polyphosphates for energy. Normal in the skin, URT, GI, UGT. Almost ALL can be opportunistic pathogens but few can cause primary infections.
   1. *Gravis*
   2. *Mitis: often with diphtheria and can acquire the prophage with the toxin*
   3. *Intermedium*
   4. *Belfanti: rarely seen in diphtheria*

Diptheria means leather and comes from the pseudomembrane stretching across the back of the throat. 1890’s there was the first antitoxin from horses and was the first proof of humoral immunity. Primarily a childhood disease and rarely seen as a cutaneous disease (only in tropical countries). **SX** PT presents with mild fever, sore throat, malaise, loss of appetite. Mucous membranes of URT are the primary target. A pseudomembrane forms over tonsils and can extend to the trachea. It is firm, fleshy, grey and adherent with full vascularization. “Bull neck” can occur from cervical swollen lymph nodes. Complications include myocarditis and polyneuropathies (rarely systemic toxicity). **Virulence:** Microbe uses a classic binary toxin from a lysogenic phage. B binds heparin-binding epidermal growth factor on host cells. Tanslocation and internalization with a pore formed which releases A to inactivate EF-2. One A can inactive an entire cell’s EF-2 molecules. **Diagnosis/TX clinical diagnosis. Selective media include: Tinsdale (tellurite to inhibit most bacterial growth while the diphtheria can reduce) or CNA(Not diagnostic). Need to detect the toxin/phage so use: Elek test or PCR. Elek test is a classic and VERY effective. The center strip is antitoxin and the known diphtheria swab is compared to an unknown swab. Simply observe a precipitant line where the toxin meets the antitoxin. Treat with antitoxin (DAT), secure airway, antibiotics to kill bacteria, prophylaxis for anyone exposed. Prevent with the vax (DTaP 4 doses and Tdap booster) NOTE the small letters mean a lesser amount and the “a” means acellular.**

1. *Cornebacterium jeikeium:*  opportunistic in immunocompromised patients (hema disorders and IV catheters). Seen in hospitalized patients and very antibiotic resistant.
2. *Cornebacterium urelyticum:* uncommon in healthy people. STRONG urease producer and lives in renal stones and struvite calculi. Also very antibiotic resistant
3. *Cornebacterium amycolatum:* opportunistic in skin but not oropharynx and commonly isolated in clinical specimens.
4. *C.* *ulcerans:* can carry the diphtheria toxin gene and indistinguishable from *C.diphtheria.*
5. *Pshedotuberculosis:* rare cause of infection but can also care the toxin gene.
6. *Arcanobacterium:* irregularly shaped bacteria; **SX** colonizer and pathogen while being associated with pharyngitis, wounds, endocarditis, septicemia. **Diagnosis/TX Penicillin or erythro**
7. *Brevibacterium:* skin colonizer with a cheese like odor (mostly feet). **SX** septicemia, osteomyelitis, foreign body infections. Is a rod when a young bacteria but morphs to a coccoid shape. **Diagnosis/TX resitance to many drugs so need vanco, tetra or gentamycin**
8. *Rothia mucilaginosa:* Major colonizer of oropharynx down to the URT. Growth in clusters and is technically a cocci (but still a corneform bacteria like the others). **Virulence** very mucoid and sticky so that it can adhere to the damaged heart valves and cause endocarditis. **SX** bacteremia, endopthalmitis, catheter infections, CNS infections, pneumonia, peritonitis and septicemia. **Diagnosis/TX Random and need to culture and run susceptibility tests.**
9. *Tropheryma whippeli:* Disordered immune response to persistent bacteria. It is hard to gram stain (use periodic acid-Schiff positive), infect macrophages, intracellular growth. Mostly older white individuals. **SX** Gastrointestinal disoroders with malabsorption, weight loss, diarrhea, joint pain, arthritis. Can also have some FA deposition in the intestines. Can also cause heart, lung, brain, joint, eye disease. Fatal after 1 year. **Diagnosis/TX PAS macrophage inclusions, IHC staining of tissues, PCR confirmation. Treat with 2 weeks of parenteral penicillin/streptomycin and 1 year of oral trimethoprim/sulfa drugs. OFTEN RELASES.**
10. *Propionibacterium acnes:* grows in short chains/clumps; anaerobic/aerotolerant; ferment carbs to make propionic acid. Most common in adolescents in the face and upper neck/back. Associated with male hormones causing acne vulgaris. **SX** infection of sebaceous follicles causing increased sebum and androgen production. Leukocytes migrate to the site creating an inflammatory lesion with scarring. **Diagnosis/TX clinical evaluation followed by topical antibiotics (erythro/clinda/tetra) or benzoyl peroxide to dry skin and increase the skin turnover.**
11. *Bifidobacterium:* anaerobic with mixed infections of the oropharynx or bowel.

**🚑 Actinomycetes: g(+) bacteria with filamentous growth. An individual member is called an actinomycete. There are three basic groups: Actinomyces, Nocardia, Streptomyces. Some produce medium chain mycolic acids with a beading pattern in gram stains and are partially acid fast. Others have no mycolic acids and are normal g(+) gram staining.**

1. *Actinomyces israelii, naeslundii, radingae, turicensis (2 weeks):* normally found in the mucous membranes of healthy people (UTR) though they can cause endogenous infections. They have no mycolic acids and stain like a regular filamentous g(+) rod. Domed irregular surface in bacterial culture (molar tooth). They have a low virulence unless the mucosal epithelium is disrupted. **SX** poor oral hygiene/dental procedures, aspiration, GI surgery/trauma, lung spread to CNS. Cervicofacial lumps from acute pyogenic infection; thoracic infection from a pulmonary infiltrate; looks like a slow growing tumor post surgery/trauma. Farmer’s lung: affects the farmers from inhalation of the dust particles and produces hypesensitivity (type III). Acute/subacute/chronic. Chronic is the worst with permanent damage leading to death in 5 years. **Diagnosis/TX difficult to culture, need bichem/PCR to analyze. Treat 6months to 1 year and resistant to most antibacterial drugs so need to just move to a clean environment.**
2. *Nocardia asteroids/brasiliensis (3-5 days):* normal external environmental contaminant with medium chain mycolic acids causing a beading pattern when gram stained. Their filamentous growth almost looks like a fungal hyphae. Colonies are white-orange. This is a very invasive microbe. **SX** cause pulmonary disease in ummunocomp, brain abcesses (30% of cases) common in t-cell deficient patients, primary cutaneous infections after trauma and subcutaneous infections (mycetoma in the feet). **Virulence** cord factor to prevent lysosomal/phagosomal fusion; prevents acidification of phagolysosome, protected by catalase and SOD, avoids phosphatase mediated killing. **Diagnosis/TX stain CSF/sputum/abscess samples, grow on a media, ID the species level by PCR. Treat with trimethoprim/sulfa drug for local infections and Amikacin and imipenem for disseminated infections.**

**IV Gram Negative: Rod (aerobic/non), Coccus, Pleomorphic, Helical/Curved**

**🚑 Rod (1,3-6 aerobic/ 2 facultative/ 7,8 anaerobic)**

1. *Legionella:* aerobic. Common community acquired pneumonia. Unique since it’s not a *Streptococcus pneumonia*e and is characterized by its possibility to have diarrhea. Bronchial wash shows thin watery secretions in the upper respiratory tract (instead of thick purulent secretions). Needs a special media to be cultured. No person-person spread, no animal reservoir, ubiquitous in MANY different water sources that hold amoeba *Harmenella vermiformis* (infect amoeba and form cysts). The amoeba is resistant to chlorine and thus protects the infected cyst Contracted by inhaling contaminated water or dust. Involved with inhibition of the mucociliary elevators. Difficult to stain. Attacks alveolar macrophages and grows within them by means of binding C3b and entering the host cell but never fusing with the lysosome. Ribosomes are recruited and the bacteria grows in a coiled phagosome. Cell lysis releases the bug. Metaloproteases breaks down the lung tissue and destroys CD4 and IL2 receptors (more than one protease though). This triggers a vigorous host immune response that is partly responsible for the lung damage. **SX** Legionnaires disease with a low rate of attack 5%, and preferentially attacks the weak. Serious permanent pulmonary damage with 15-20% mortality if treatment delayed. Pontiac fever: high attack rate, self limiting, low mortality. **Diagnosis/TX Buffered charcoal yeast extract (BCYE) makes a great medium as the charcoal takes out the aromatic molecules that inhibit growth. Colonies form in 3-5 days but can be up to 2 weeks. ELISA patient urine to detect serotypes. CDC recommends a sputum and urine ELISA. Often misdiagnosed because hard to see, forgot to test and the tests are not very good. Treat with drugs that can enter the macrophages. Use Macrolides, fluoroquinolones and sometimes rifampin.**

NOTE: Protazoans graze on bacteria. Pre ingestional adaptations- oversized, fast, surface masking, biofilm, toxins. Post ingestional adaptations- digestion resistant (staph and TB), toxins, intracellular growth (Myco avium, listeria, chlamydia, Legionella…)

1. *Enterobactericeae:* facultative aerobes. Motile (except shigella, klebsiella, Yersinia), fermenting bacteria classified by their serotypes. Major types are based on their H (flagella), K (capsule), O (surface LPS) proteins. (a-e are non enteropathic) (f-i are enteropathic)
   1. *E.coli K1:* mucosal colonization, invasion of the bloodstream, multiply and cause high levels of bacteremia, cross BBB. K1 capsule (polysialic acid like Neisseria) is responsible for binding and causing internalization of bacteria in brain microvascular endothelial cells. Also use PMN cells in early replication where the PMN spread to distant sites and infect macrophages (OmpA causes cells to increase the gp96 on PMN) Seen in infants **SX** acute fever, poor feeding, bulging anterior fontanelle. CSF had Ecoli. Post treatment can show neurologic sequelae. **Virulence** K1 binds factor H to prevent complement, polysialic acid evades host by mimicry of host NCAM. **Diagnosis/TX CSF WBC, protein, glucose all suggest a K1 infection as well as a gram stain of the CSF. Blood cultures often positive for the same ecoli. Treat with IV antibiotics: broad spectrum cephalosporin and aminoglycosides.**
   2. *Uropathogenic E.Col (UPEC)i:* **SX** woman with cystitis (95%) or pyelonephritis (5%). Pain on urination, frequent urination, suprapubic pain (sex, contaminated food, oral/anal)… OR chills high fever, nausea, myalgia, flank pain (leads to renal failure, bacteremia and shock). **Virulence** Type 1 pili for adhesion, pyelonephritis pili (PAP or P-fimbriae) and other adhesins. Once bound, cellular apoptosis with exfoliation, dormant intracellular, reactivation. Siderophores, alpha hemolysin (modulate inflammatory and trigger apop).
   3. *Proteus mirabilis:* swarming motility due to hyperflaggelated/urease-producing microbes. The microbe uses urease to degrade urea into a usable nitrogen source. The byproduct of the urease, is an insoluble carbonate that can form calcium/carb deposists infected with the bug. **Diagnosis/TX urinalysis for different urine contents (protein, nitrogen, ketones…) microscopic analysis for crystals and microbes. Treat both UPEC and Proteus with fluoroquinolones and aminoglycosides for serious infections.**
   4. *Klebsiella pneumonia:* K1 serotype is the most common (nothing to do with the E.Coli Serotype). Mucoid colonies that are non-motile, lactose fermenting and have urease. **SX** pneumonia, UTI, bilieary tract infection, wound infection, ocular/neuro infections. Pneumonia comes with high WBC, patchy opacity in the lungs, blood tinged/think sputum (currant jelly) with g(-) rods. **Virulence** the capsule is the major virulence factor with its thick polysaccharide layer (antiphagocytic and prevents complement). LPS causes sepsis, adhesins and siderophores. **Diagnosis/TX use whole chromosome sequencing in outbreaks. Extended spectrum B-lactams and newer cephalosporins with aminoglycosides.**
   5. *Yersinia pestis:* oriental rat flea (infected flea has a clogged gut which increases its need to feed causing it to bite multiple hosts and vomit out contaminated stomach contents into the wound). Relative of the *Y.pseudotuberculosis* or the “black death” or “bubonic plague”. Non-motile **SX** buboes eyes, necrotic secondary to dissemination. Fever, tachycardia, increased RR, small mass at the site of the bite, small hemorrhages across skin. **Virulence** Outer proteins (Yop) block phago, reseal host membrane, block platelet activation. Bind to APC cells where it will be transferred to lymphocytes for dissemination. Its primary method is to infect and be silent for 36hrs suppressing the immune system (increasing the risk of 2ndary infections) before activating a strong inflammatory response and killing the host. **Diagnosis/TX clinical presentation, Wright stain preferentially stains the granules at the ends of the bacteria causing a characteristic “safety pin” appearance. Treat with streptomycin (outside US), gentamycin, doxy, chloramphenicol. NOTE: bubonic has a decent cure rate with treatment, septicemic has a 60% and pneumonic has a <10%. FYI They have found drug resistant plague!!!**
   6. *EPEC Enteropathogenic Escherichia coli:* causes outbreaks of diarrhea in nurseries and does not involve exotoxins (its shiga-like endotoxin is not very pathogenic). No inflammation or fever as the diarrhea is mediated by a decrease in aquaporins, and altering actin pol in microvilli resulting in an effacing lesion with pedestal. **Virulence** loosely bind via fimbrial adhesin and tightly bind via intimin (OMP which binds to Tir)
   7. *EHEC Enterohemorrhagic Escherichia coli:* Grows in the terminal regions of the colon, does not invade the blood, attachment proteins like EPEC and have filaments and pilus that may transfer the toxin to cell. **SX** nonfebrile bloody diarrhea from hemorrhagic colitis (O157:H7 serotype causes 50% of the infections). Acid resistant like shigella. Not terribly fatal unless you develop hemolytic-uremic syndrome HUS (10% of cases) which leads to acute renal failure. The renal failure is mediated by the shiga-like endotoxin. #1 cause of acute renal failure in children. From food contamination, swimming pools and animal contact. HUS causes fever, thrombocytopenia, hemolytic anemia and schistocytes. URT and viral diseases can also cause HUS. **Diagnosis/TX Symptoms and serotyping. Antibiotics are NOT recommended and oral rehydration is usually sufficient. If HUS develops, need blood transfusion, electrolytes, IV fluid and dialysis. NOTE a recent disease was found in Germany to have Aggregative and Hemorrhagic qualities since a phage had transferred the shiga toxin from EHEC to EAEC to make EAHEC.**
   8. *Salmonella:* Non typhoidal salmonella and typhoid fever. Part of the normal flora of many animals and is spread by fecal oral spread. Acid sensitive and travel to the ileum and colon where they attatch and penetrate the mucosal barrier. Use invasion to force phagocytosis. They do not remain in the epithelial cells but pass into the blood to multiply in the macrophages of the liver and lymph nodes. Once a threshold is reached, they are released back into the blood (secondary bacteremia) where they cause the continuous bacteremia and daily fevers for 4-8 weeks. Infected individuals:
      1. Carriers
      2. Gastroenteritis: *S.enterica* causing N/V/D (from chicken)
      3. Vascular endothelial infection: *S. choleraesuis, typhimurium*
      4. Typhoid fever: *S.typhi* and *paratyphi AandB (*human carrier)
      5. Particular ogan infection: *S.typhimurium* causing osteomyelitis in sickle cell

**Virulence** invasion forces the enterocytes to take them up. The biofilm helps them to remain in the gall stones of individuals causing recurring infection. The interaction of gastroenteritis producing salmonellae cause an active inflammatory response and direct damage to mucosa. The other more virulent strains can grow in macrophages allowing them to spread and infect different tissues causing endocarditis and vascular infection. **Diagnosis/TX history of being outside the US, specific growth media can allow colony formation, serology can tell the strain. Gastroenteritis is not always treated with antibiotics. Typhoid fever is always treated with antibiotics since active infection causes damage directly and is not self-limiting. Fluoroquinolones can be used but there is increasing resistance.**

* 1. *Yersinia entercolitica:*  several countries and now more prevelant than Shigella. **SX** Causes acute bacterial gastroenteritis. Invasive microbe (like other Yersinia) and causes its disease by directly inflicting tissue damage. It specifically targets the peyer’s patches of the ileum. In rare cases, it can cause bacteremia by spreading to the mesenteric lymph nodes and has a 34-50% mortality rate. Spread by contaminated water/food. **Virulence** inability to chelate iron (no siderophores) but can use the siderophores from coinfecting bacteria. Can grow at 4C and can mimic appendicitis. **Diagnosis/TX causes dysentery and needs antibiotic treatment (not necessarily rehydration)**
  2. *Shigella dysenteriae(1-7 days):* (Esentially is Ecoli with a large virulence plasmid due to divergent evolution) invade, damage the colon mucosa causing bloody diarrhea with puss. Very acid stable and similar to *EIEC Enteroinvasive Escherichea coli.* Person to person contact and sometimes from a contaminated source. Bacteremia is uncommon though the shiga toxin is the cause**SX** Dysentary is characterized by frequent passage of low volume stools with blood and pus. PT have cramps and pain from straining. This infection is serious and can be life threatening and is especially common in children. Four serotypes (A-D) and A can produce severe neurologic problems with 40% of children partially because of shiga toxin. **Virulence** microbe enters the M (microfold) cells of the colon by invasin binding to an integrin. They then pass into the lamina propria where some are ingested by macrophages which release IL-1 (crucial for the host to cause pathogenic diarrhea). The inflammation loosens the tight junctions increasing the permeation by the microbe and attachment to the basolateral aspect of the epithelial mucosal cells for endocytosis (hemolysin allows to escape phagosome). Actin based motility to spread to neighboring cells (like listeria, burkholderia). Shiga toxin halts 60S ribosome. **Diagnosis/TX serotyping and PCR are good diagnostic tools as well as culturing fresh feces. Treat with fluoroquinolones. NOTE see Listeria in g(+) non-sporulating rods as an example of convergent evolution.**

1. *Psuedomonas aeruginosa:* **Embodies opportunistic bacteria.** Lactose/glucose non-fermenting, oxidase positive rod that is a nosocomial pathogen. It is motile and hemolytic and can grow everywhere. It easily forms biofilms or lives in a planktonic form. High metabolic versatility seen at various temps (mostly 37C). **Virulence:** fimbrae, proteases, alginate (a mucoid adhesion that is protective and makes up the capsule/exopolysaccharide/glycocalix), hemoysin, pyocyanin (impair human cilia), LPS. Exoenzyme S takes proteins while Exotoxin A has the same mechanism as diphtheria and kills EF2. Needs to have skin damage to infect because it is opportunistic. **SX** UTI, CF pneumo, Skin infection in burns, Bacteremia, Endocarditis, Ear infections. **Diagnosis/TX: use odor (fruity) and pigmentation: the bacteria produces pyoverdin (fluorescent under UV and somehow involved in iron metabolism) and pyocyanin which colors the pus blue. Treat with fluoroquinolones, aminoglycosides and third gen B-latams. Notoriously resistant because of the transmissible resistance plasmids, LPS layer, cohabitation in the dirt with other bugs so resists most natural antibiotics. NOTE: need a better vax (polyvalent conjugate vax is showing promise for CF), new antibiotics targeting quorum sensing or biofilm, increasing the local oxygenation, target virulence.**
2. *Burkholderia mallei:* causes glanders and is a very close relative of psuedomonas
3. *Burkholderia pseudomallei:*  causes melliogosis
4. *Burkholderia cepacea:* same disease as *P.aeruginosa* although less pathogenic in UTI and septicemia though more pathogenic in CF patients. **Can be treated with trimethoprim/sulfa drug even though the cultured form of the bacteria is resistant.**
5. *Bacteroides:* anaerobic, bile resistant, part of natural flora. SOD and catalase positive. Ferment carbs that can be used by the host for energy.
   1. *B.fragilis:*  less than 1% of the natural flora but the most common anaerobic pathogen. **Virulence:** capsule enables it to form abscesses with pyogenic inflammation and offers resitance to phago/complement. LPS with low toxicity (yet can still causes tissue damage). Mostly found in polymicrobial anaerobic infections. Enters tissue after a rupturing event. Needs a facultative anaerobe to take up most of the O2 in the env. **Diagnosis/TX Gram stain in anaerobic conditions shows variable colony morphology with growth in bile and kanamycin/vanco/colistin. Treat for facultative anaerobes (gentamycin) and strict anaerobes (metronidazole).**
6. *Prevotella:* female genital tract or URT. Mixed infections
7. *Fusobacterium:*
   1. *F. necrophorum*: round ended long rods. Causes lemierre’s disease with acute jugular vein thrombosis leading to sepsis. Also abscesses all over the body
   2. *F*.*nucleatum:* needle shaped ends. Part of the gingival microflora. Some genital, GI, URT, brain infections.
8. *Porphyromonas:* normal oral flora and seen in gingival and tooth infections. Can also be seen in breast, axillary, perianal, male genital infections.

**🚑 Pleomorphic rods**

1. *Rickettsiaceae:* obligate intracellular (target endothelial cells), stains poorly due to thin PG layer, and small amounts of LPS. Maintained in animal and arthropod reservoirs. They can perform anaerobic glycolysis and can grow in the cytoplasm or nucleus of infected host cells. They stimulate endocytosis (OmpA) and use phospholipase to escape the endosome. Spotted fevers utilize actin polymerization while the typhus bugs rely on apoptosis.
   1. *R.rickettsii (5-10 days after a 48hr tick bite):*  also known as “Rocky Mountain Spotted Fever” or Black measles with increased prevelance in African Americans and American Indians. Mortality is 30% without treatment. Rash comes 2-5 days after fever which makes it harder to treat. G6PD, alcohol, male, advancing age and ethnicity all play a role. Increasing in prevelance in the South with *dermacentor variabilis* ticks (dog ticks and wood ticks). **SX** acute onset rash (spots that turn pale and are not painful/itchy) starting on the palms and feet moving towards the chest, fever, headache, and history of tick bite. Vomitting and sepsis begin to set in with edema, hypovolemia, hypotension and low albumin. Cyanosis, darkening of the rash (necrosis or gangrene), thrombocytopenia, cyanosis and seizures leading to death in youths. **Difference from Ixodes:** multiple bites, male ticks can infect females, female can transfer to eggs. They carry the pathogen for life. **Diagnosis/TX: Weil-Felix, indirect immunofluorescence, PCR. Treat with doxycycline**
   2. *R.akari(1-2 weeks): “*rickettsialpox” in the urban areas with sporadic cases throughout the US. Mites carry this microbe and the disease is biphasic. **SX** papule that develops into an eschar. Headache, chills, rigor, sweating, myalgia and rash. Lower morbidity and similar presentation to ricketsii. **Diagnosis/TX almost indistinguishable from ricketsii and treat the same.**
   3. *R.prowazekii (1-2 weeks):* known as “epidemic typhus” and occurs in the colder/overcrowed/unsanitary populations. Transferred by the louse and may be held in a flying squirrel reservoir. Rash develops in the reverse order from rocky mountain fever and comes from the 4-7th day. Higher mortality with the possibility of recurrence. Does not utilize the actin polymerization and relies on apoptosis. **SX** flu like symptoms with a rash. Significant mental impairment, stupor, and renal failure. **Diagnosis/TX Africa, SA, Asia. Doxy?**
   4. *R.typhi (1-3 weeks): “*Endemic/murine typhus”. Natural reservoir in rodents with transmission by fleas or rat louse. Subtropical regions are the primary, but also in California or southern Texas. Same as epidemic typhus. **SX** flu like symptoms, abdominal pain and vomiting. Black eschar with rash on the trunk to the limbs and variable morbidity.
2. *Coxiella burnetii (LONG TIME with potential for chronic):* found in Australia and called “query fever” with ticks being the important vector from livestock. SCV: metabolically inactive and spore-like. This extracellular form is attatched to cells and then actiavates. LCV: metabolically active and replicating. This form is protected from antibodies since it is inside the host cell. Aerosols are the main route of infection. Doesn’t cause disease in animals and disease in 50% of infected people. **SX** long incubation with sudden acute onset of high fever (104-5), severe headache, malaise, myalgia, V/D with fever for 1-2 weeks. 30-50% with atypical pneumonia and often hepatitis. Most self resolve and few die. Chronic symptoms can occur long after initial infection and often cause endocarditis. Most of the chronic will die from the disease. **Diagnosis/TX: Serologic testing of the two antigenic phase LPS. Phase I (smooth) LPS associated with chronic and has IgG. Phase II (rough) LPS is associated with acute and has IgM. Treat with Tetra or multiple drugs if endocarditis. Some vax but not in the US. NOTE: this could also be used as a potential bioterrorist microbe.**
3. *Bordatella:* multiple types of which the pertusis is the most common and the most virulent in humans. Respiratory droplets though the actual airborne route is rare for transmission. Maximal communicability stage is in the catarrhal stage. **Chronic cough in adults and late teens could be pertusis since the immunity wanes after vax.** 
   1. *B.* *bronchiseptica:* primarily animal infections, motile, has PT but doesn’t produce
   2. *B.parapertusis:*  humans and sheep, non-motile, no PT, mild disease
   3. *B.holmesii:* human sepsis
   4. *B. pertusis:* only in humans, motile, PT, whooping cough, obligate aerobe, fastidious (Bordet-Genjou or Regan Lowe). Toxin mediated though inflammation interferes with host’s ability to clear pulmonary secretions. Never enters the respiratory epithelium but sits in the cilia. **SX: Catarrhal stage, paroxysmal stage, convalescent stage (all totaling 100dys.)** Nonspecific symptoms that turn to predominant whooping cough (paroxysms, post-tussive emesis, whoop) moving to relapse with small recurrences. NOTE neonates get from their mother shortly after birth. Elderly can also contract the bug but usually do not have the “whoop”. **Complications:** pneumo, seizures, encephalopathy, death, hemorrhage

**Virulence:** filamentous hemaglutinin (used in vax), fibrae for humoral immunity, pertactin (increased protective immunity), PT is an AB toxin where A causes lymphocytosis by ribosylating Gi and increasing insulin. **Diagnosis/Treat: best to do symptoms, xray, PCR/culture in early stages and Serology in the late stages. PCR is really the best option though. Macrolides are the best treatment but also erythromycin for prophylaxis and also be sure to give supportive care for the infants/toddlers.**

1. *Pasteruellaceae:*  large family of random bacteria often associated with animal bites. *Haemophilus, pasteruella, actinobacillus, aggregatibacter* are all non-motile, fastidious (need enriched media), facultative anaerobes. P=dog/cat bites, A=rare with bacteremia/meningitis from bite, AG=new, rare, cause endocarditis.
   1. *Haemophilus ducreyi:* STD in other countries
   2. *Haemophilus aegyptius:* pink eye
   3. *Haemophilus parainfluenza:* bacteremia and endocarditis
   4. *Haemophilu influenza:* Encapsulated: meningitis in kids under the age of 2 (type B). Unencapsulated: non-pathogenic colonization, OM, sinusitis. Chocolate media needs X(hemin) and Y(NAD). **Virulence:** Capsule, LPS, IgA protease, Adhesins. Increased risk in immunocompromised and patients without a spleen. **Diagnosis/TX: specimen collection, microscopic analysis, culture. Administer cephalosporins (can do macrolides or FQ but do not work as well). Vax is a synthetic oligosaccharide linked to a tetanus toxoid and can be given as early as 6 weeks (usually give with the DTap at 2,4,6,12 months).**
2. *Francisella and brucella:* most damage from immune system, highly invasive in immunocompromised, grow in macrophages, grow poorly in lab, zoonotic, cause lab diseases and could be used for bioterrorism. Think Midwest USA and martha’s vineyard in Massachusettes for F and Mediterranean, middle east and cattle exposure for B.
   1. *F.tularensis:* tularemia is a category A agent on the CDC list since it has high mortality, could cause public panic and easily disseminated. Fran is its own family of two species where tularemia is the most important. Type A and B are the most virulent subspecies. Non-motile, lives in dead carcasses, needs cysteine chocolate agar and is a strict aerobe. Type A is exclusively in North America where the eastern form A-1 is the disseminated form has the highest mortality. Type B is in various places and is less virulent. Mostly infected from a tick or contact with infected animal (rabbits then cats). **Virulence** It has a capsule that binds complement but does not get lysed. Pathogenicity island of genes with lower GC content indicate horizontal transfer, needed for intracellular growth/phagosome excape. Also produces a non endotoxic LPS that does not stimulate TLR4 (this is a 4 acyl chain with 16-18 carbons long with sugars instead of phosphates). Stealth entrance into the host cell (maybe by complement). **SX** Acute is 3-5 days of flu like symptoms and erythema nodosum (shins) or bubos leading to Prolonged disease with cough/chest pain/ liver liquification. **Ulceroglandular (most cases), Glandular, Oculoglandular, Oropharyngeal (ulcers through GI), Pneumonic all leading to Typhoidal if they do not resolve by day 6. Pneumonic and Typhoidal have 60% mortality.** Silent asymptomatic initial attack that infects macrophages. **Diagnosis/TX: Microscopic (poor), culture of scapings/biopsy (submit colonies to agglutination), serology (not good since no Ab till atleast 4wks). Treat with Ciprofloxacin for 14 days. There is a “vax” but not really used**
   2. *Brucella*sp(2-4wks): Bang’s disease that does not have a capsule, has a non-motile flagella, complex media, metabolize erythritol (placenta, breast, uterus, epididymis). Infects macrophages. Produces Urease and LPS that alternate where smooth is virulent but still less virulent than most g(-). LPS has 6 acyl chain with 28 carbons to evade TLR4 and block apoptosis in macrophages. O antigen group block C3 binding and block MHCII in macrophages. Four species cause disease in humans: *B. melitensis(most common), B. abortus, B. suis, B. canis(least common).* Most common zoonosis worldwide. Contact with abraded skin, inhalation, injestion all confer the disease. **SX Undulating fever, malodorous sweat, arthralgia.** Causes sterility and abortion. Often associated with drinking unpasteurized dairy (49 states are brucella free as of now). Vets, lab workers, hunters, travelors are all at risk. Acute form shows nonspecific flu like symptoms with undulating fever, malodorous sweats, myalgia (<8wks). Undulant form with intermittent fevers, infertility/abortions, arthralgia (<1yr). Chronic displays chronic fatigue syndrome, depression, arthritis, hepatosplenomegaly, endocarditis (rarely but VERY severe). **Diagnosis/TX Culture is the best method but the LPS agglutination test can be cross reactive for Yersinia, Vibrio, Ecoli, Francisela . Culture. Treat with Doxy/Strep for 3wks or Tetra/Strep for 6wks. There is an animal vax which people can accidentally give themselves (RB51 vax needs doxy/strep)**

**🚑 Curved/Helical**

1. *Heliobacter pylori:* 45% of population has this bacteria in the stomach of which 70% will possess a pathogenic infection. High correlation with gastric ulcers and gastric carcinoma. Several polar flagella with corkscrew motility like spirochetes. Fecal-oral or oral-oral spread especially in developing countries where 90% of people are infected by the age of 10. **Virulence:**
   1. Urease to raise the PH
   2. Flagella to move quickly to the musin layer of the stomach
   3. Corkscrew motility to move through the mucus
   4. Mucinase/phospholipase to reach the epithelial mucosal cells
   5. Adhesins to bind and resist the outflow of the mucin into the small intestine
   6. Immune evasion: catalase, SOD, low toxicity of LPS, immunogenic LPS, VacA (inbit Tcell proliferation and B cell Ag presentation)
   7. DAMAGE: ammonia, VacA, inflammation, NAP (activates neutrophils), CagA to activate NF-kB

Carcinoma: chronica atrophic gastritis leads to cancer (CagA associated with cancer). Can also cause lymphoproliferative disease. These links are poorly understood. **Diagnosis/TX urease test (non-invasive), culture (3days at 37C), PCR, fecal antigen test of stool…. Give proton-pump inhibitors with 1-2 weeks of antibiotics (monitor for C.difficile)**

1. *Camplobacter jejuni (2-5 days):* #1 cause of bacterial gastroenteritis in the US. No urease, one flagella and culture at 42C.**SX** fever, abdominal pain, mimics appendicitis, bloody diarrhea. Self-limiting since only lasts 1 week. Does not spread person to person but often in contaminated food and water. **Virulence**: mucosal surfaces appear ulcerated and bloddy. Cytolethal distending toxin (CDT) is a DNAase but not the only answer. Capsule provides immune evasion, LOS provides immune evasion and tissue damage (guillian barre since the LPS looks like the myelin ganglioside). **Diagnosis/TX ELISA for common AG, Gram stain, culture stool sample (3 days at 42C). Treat by keeping hydrated and erythromycin/azithromycin .**
2. *Vibrio cholera (2-4days):* comma shaped rod, long polar flagellum, facultative anaerobe. Contaminated shellfish are a common source of infection. **SX** watery diarrhea with mucus, severe dehydration. 60% mortality without treatment. Metabolic acidosis, hypokalemia, seizures, survivors will become immune. **Virulence** O1 and O139 serotypes with ctxAB genes regulating the endotoxin production and cause “cholera”. B binds the ganglioside on intestinal cells and A is internalized where it alters the regulation of CAMP. ADP ribosylation of Gs protein causes the adenylyl cylase to always produce cAMP leading to hypersecretion of water. Neuramidase changes the host cell’s surface GM1 to increase its binding to toxin. Zot and Ace are the toxins responsible for a less severe diarrhea in other ctx- strains. VERY acid sensitive so need to have large numbers. **Diagnosis/TX diagnosis by PCR and clinical symptoms. Need urgent treatment for dehydration and can give antibiotic to reduce the spread to the rest of the population.**
3. *Vibrio parahaemolyticus:* **SX** explosive diarrhea in 24 hrs with N/V and abdominal cramps. Headache, low fever and self limiting. It is the #1 cause of seafood gastroenteritis. Hemolysin is responsible for the chloride secretion and tissue damage
4. *Virbrio vulnificus:* **SX** diarrhea, N/V and cramps. Problematic in immunocomp patients with bacteremia, fever, chills, skin leasions (even necrotizing fasciitis). **Virulence** Cytolysin/hemolysin cause the pores in eukaryotic cells leading to tissue damage. Metaloproteases aslo cause tissue damage while sideropores sequester iron and RtxA toxin is a cytotoxin. #1 cause of seafood related deaths. **Diagnosis/TX treat with doxycycline and fluoroquinolones/cefotaxime.**

NOTE: all the vibrio microbes come from some contaminated source and have physiologic effects mediated by their toxins. The vulnificus can cause necrotizing fasciitis by its capsule and has a high mortality rate.

**🚑 Chlamydiaceae:** unique family of g (-) which do not have PG (have disulfide linked envB) and are incredibly small. They do still have PBP but can’t be gram stained or given B-lactams. They are obligate intracellular (used to think they were viruses) and can’t really make their own ATP. Unique development in that they have EB elementary bodies (spore like) and RB reticulate bodies. EB is small, electron dense nucleoid and highly crosslinked EnvB. Glycosaminoglycan on host allows to bind, become endocytised and germinate to the RB. The RB is non-infectious, metabolically active and replicating by binary fission. EB -> RB -> EBs (72hrs). These show high rates of reinfection with little antibody protection.

1. *Chlamydia trachomatis:*  two forms are Thrachoma and LGV.
   1. Trachoma A-C causes conjunctivitis. This is called “trachoma” and is not the same as the STD. Personal contact with discharge from the eyes, clothing, flies, vaginal delivery all result in contamination. It is a disease of poverty and unsanitary living conditions. Women have traditionally been more likely to contract the disease. **SX** entropion and trichiasis are the primary symptoms that lead to scratching of the cornea/scarring and eventually cause blindness. WHO has instituted a world-wide campaign called SAFE (surgery, antibiotics, face-washing, environment cleaning)
   2. Trachoma D-K causes the “clam” (STD) and has relatively less secretions than gonorrhea. 75-85% of cases are asymptomatic. Can cause PID in woman and could be passed to infants causing conjunctivitis. The trends show a predominance in the South east. Screening should be done for any young sexually active females. Transmitted sexually and infects the single-cell columnar layers (endocervix in women or urethra in men). **SX** intense inflammation, redness, oedema, discharge. Mucopurulent cervicitis or non-gonnococcal urethritis. Buring during urination or unusual discharge are the normal symptoms. 75% of women are infected and 25-50% of men. Often coinfects with N.gonorrhoeae. Reiter’s Syndrome is a complication with “can’t pee, can’t see, can’t climb a tree”. Reactive arthritis with a good recovery rate once the bacteria is eradicated.
   3. LGV enters through the epithelial cells in the mucosal membranes. Painless herpetiform ulcer at the point of inoculation. Travels in the lymphatics to multiply in MNP (inguinal syndrome in men). A tertiary stage of infection can occur YEARS after the primary infection where you have anogenitorectal syndrome (rectal stricture or elephantiasis of genitals). Mostly in Africa/SA in homosexual men.

**Diagnosis/TX Isolate, culture in human epithelial cell lines. IFA, ELISA, Nucleic acid based tests (PCR). Treat with doxycycline (7days) or 1 azithromycin. Trachoma can use topical applicants but LGV needs a longer dose of doxy (BID 21dys). Treat sexual partners and realize the antibiotics only work on the RB.**

1. *Clamydophila psittaci (1-2 wks):* contracted by inhaling bird feces. **SX**  mild symptoms or even asymptomatic. Can cause a non-productive cough, CNS issues, headache… can spred to the liver/spleen and cause focal necrosis.
2. *Clamydophila pneumoniae (TWAR):* pear shaped EBs with large periplasmic space (not so rod shaped). Respiratory secretions are the primary method of spread and humans are the only known reservoir. **SX**  most are asymptomatic (50% of adults have an antibody against) but can have walking pneumonia with persistant cough and not super serious. Could be linked to atherosclerosis??? **Diagnosis/TX few good tests but can be treated with antibiotics that can enter host cells.**

**🚑 Coccus: Neisseriaceae has Neisseria, Eikenella (opportunistic after fist fights/human bites), Kingella (normal inhabitant that can cause arthritis/endocarditis). Moraxella is the other group.**

1. *N.gonorrhoeae:*  non-motile, diploccoci aerobe that is somewhat fastidious (Thayer-Martin agar needed). They are oxidase and catalase positive and both G and M share most of their virulence factors. **Virulence** a IV pilus that lets them bind to CD46 on non-ciliated epithelium. Opa proteins to promote binding to various host cells. Release PG fragments to kill the ciliated cells, Por proteins to facilitated infusion of epithelial cells, interfere with neutrophils and resistance to compement. Also have receptors to directly take up the iron from host so that they do not need siderophores. LOS has endotoxin activity to activate inflammation, IgA protease cleaves the Ig and covers the microbe, evades complement with factor H and hide in neutrophils. **SX** penile discharge, asymptomatic in women, can cause PID and in children it can cause blindness, joint infection and septicemia. Mostly in the South east especially among African Americans. IF it disseminates, it can cause bacteremia with skin lesions that are painless and the bacteria cann’t be cultured from these. Also will cause polyarthralgia with complement defficiency **Diagnosis/TX symptoms, gram stain the discharge, culture on chocolate agar and PCR. Treat with 3rd gen Cephalosporins (Ceftriaxone) and Doxycylcine or Azithromycin for a coinfection of chlamydia**
2. *N.meningitidis (3-4days):* cause meningitis (50% of infections) with sequelae in the survivors (MR, stroke, seizures, deafness), 10% lose a limb and most cases between the age of 0.5-2 years old. Seasonal peaks and most epidemics occur in individuals over the age of 2. Meningitis belt in the sub-Saharan African countries. Reservoir is the nasopharynx of humans. Transmitted by respiratory drops. Risk factors are smoking, age, crowded living conditions, complement deficiencies… **Virulence** primary virulence is due to the cap which is resistant to phagocytosis, complement, intracellular killing. Also has sialic acid polymers to sequester factor H and BCY serotypes most common in USA while the A is the most common world wide. The most successful microbes have capsules that allow survival in the blood stream. **SX** fever, headache, altered mental statis, 100% mortality if not treated. Can cause fulminant sepsis with 18-53% morbidity which is characterized by a skin petechial lesion/purpuric rash. **Diagnosis/TX isolation from a sterile site, agglutination for antibodies/PCR. Vax for everyone and has 4 capsular proteins that imbue 85% immunity with virtually no side effects. To very good with children, not a conjugated vax, no long term immunity, no serotype B, no herd immunity. 2005 a meningococcal conjugated vax now available to everyone that looks more lasting and effective. MCV4 given at 11 and 16 and then never again unless otherwise indicated.**
3. *Moraxella catarrhalis:*  human specific, diplococcic, oxidase positive, non-encapsulated, seen in PMNs. 15-20% of Otitis media and 30% of bacterial exacerbation of COPD.
4. *Acinetobacter baumannii:* diplococcic short plump rods (this species is 80% of Acineto infections). Normal flora that are in the oropharynx and skin. Aerobic and forms a biofilm with pilus and exopolysaccharide. LPS is a potent inducer of inflammation. Opportunistic in immunocomp PTs. Seen in burns, combat injuries, UTI catheter, Diabetes, chronic lung diseases (wound, septicemia, pneumonia). Very antibiotic resistant. **Diagnosis/TX Suspicion and susceptibility tests indicate a treatment of sulbactam with ampicillin or aminoglycosides; can use polymyxin E.**

**🚑 Coccobacillus: poorly staining zoonotic bacteria.**

1. *Bartonella:* Warthin-Starry silver staining of lymph nodes (brown on yellow background). Fastidious with growth at 34-37 and low CO2. Do not seem to cause disease in the animal hosts, animal arthropod resevoirs with the unique ability to cause vasoproliferative lesions in the end host. In the host, the bacteria infect the endothelium then the RBC 5 days later and at 5 day intervals relese their progeny to reinfect the endothelium or more RBC. Eventually they stop replication and persist. They form an invasome in endothelial cells with a IV secretion and actin bundling to form a protrusion.
   1. *Henselae* ***flea****:* cats in warm humid areas, CSD, Bacillary angiomatosis, peliosis, endocarditis
      1. *CSD:* perinoad’s occuloglandular disease with enchepalitis
      2. *BA:* immunosuppressed with lessions, flu, headache (erythro/doxy)
   2. *Quintana* ***louse:*** trench fever, endocarditis, chronic bacteremia, BA, shin pain and cycling symptoms every 5 days.
   3. *Bacciliformis* ***sandfly****:* oreya fever (acute) verruga perauna (chronic) make up Carrion’s disease that starts as acute febrile anemia with 40% mortality and ends as a vasoproliferative erupting skin syndrome with chronic bacteremia
2. *Anaplasmataceae:* infect macrophages, neutrophils and live with as a morulae. They are biphasic like coxiella and chlamydia and could be mistaken for RMSF
   1. *Ehrlichia chaffeensis* ***Lone star Tick:*** human monocyte ehrlichiosis HME with N/V/D, lymphadenopathy and spleenomegally. It has shin pain and increased mortality
   2. *Ehrlichia ewingii:* all other ehrlichiosis like *E.canis*
   3. *Anaplasma phagocytophilum* ***Black legged tick****:* human granulocyte anaplasmosis HGA with severe febrile illness
   4. *Neorickettsia sennetsu:*  not in the USA and very mild
3. Babesiosis **black legged tick**: a eukaryotic protozoa that infects RBC. Non specific